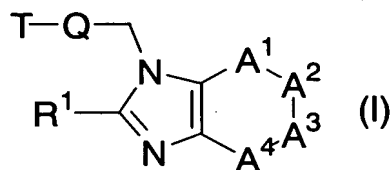


# Claims

1. A preventive and/or therapeutic agent for neutrophilic inflammatory diseases which comprises, as an active ingredient, a bicyclic heterocyclic compound represented by formula (I):



[wherein R<sup>1</sup> represents a hydrogen atom, halogen, cyano, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, a substituted or unsubstituted aliphatic heterocyclic group, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl)];

A<sup>1</sup>-A<sup>2</sup>-A<sup>3</sup>-A<sup>4</sup> represents CR<sup>2</sup>=CR<sup>3</sup>-CR<sup>4</sup>=CR<sup>5</sup> (wherein R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> are the same or different and each has the same definition as R<sup>1</sup>), N=CR<sup>3</sup>-CR<sup>4</sup>=CR<sup>5</sup> (wherein R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> have the same definitions as described above, respectively),

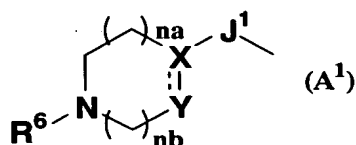
$CR^2=N-CR^4=CR^5$  (wherein  $R^2$ ,  $R^4$ , and  $R^5$  each have the same definition as described above),  $CR^2=CR^3-N=CR^5$  (wherein  $R^2$ ,  $R^3$ , and  $R^5$  have the same definitions as described above, respectively),  $CR^2=CR^3-CR^4=N$  (wherein  $R^2$ ,  $R^3$ , and  $R^4$  have the same definitions as described above, respectively),  $N=CR^3-N=CR^5$  (wherein  $R^3$  and  $R^5$  have the same definitions as described above, respectively),  $CR^2=N-CR^4=N$  (wherein  $R^2$  and  $R^4$  have the same definitions as described above, respectively), or  $N=CR^3-CR^4=N$  (wherein  $R^3$  and  $R^4$  have the same definitions as described above, respectively);

Q represents substituted or unsubstituted phenylene, substituted or unsubstituted naphthylene, substituted or unsubstituted heteroarylene, or a divalent group formed by removing any one hydrogen atom from an aliphatic heterocycle of a substituted or unsubstituted aliphatic heterocyclic group;

T represents (i) formyl, (ii) substituted or unsubstituted lower alkyl, (iii) substituted or unsubstituted lower cycloalkyl, (iv) substituted or unsubstituted lower alkanoyl, (v) substituted or unsubstituted lower cycloalkylcarbonyl, (vi) substituted or unsubstituted aryl, (vii) substituted or unsubstituted aralkyl, (viii) substituted or unsubstituted aroyl, (ix) a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl), (x) substituted or unsubstituted

aromatic heterocyclic carbonyl (wherein an aromatic heterocyclic moiety of the aromatic heterocyclic carbonyl is not tetrazolyl),

(xi) formula (A<sup>1</sup>)



[wherein na represents an integer of 0 to 3,

nb represents an integer of 1 to 4,

J<sup>1</sup> represents a single bond or carbonyl,

X--Y represents CR<sup>7</sup>-CH<sub>2</sub> (wherein R<sup>7</sup> represents a hydrogen atom, halogen, nitro, hydroxy, cyano, trifluoromethyl, formyl, lower alkyl, lower alkoxy, lower alkoxy carbonyl, lower alkanoyl, lower cycloalkyl carbonyl, or lower alkoxy carbonylamino) or C=CH,

and R<sup>6</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkyl carbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl)],

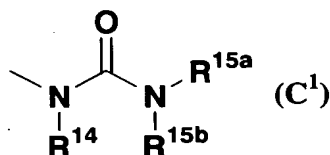
(xii) -NR<sup>11a</sup>R<sup>11b</sup> [wherein R<sup>11a</sup> and R<sup>11b</sup> are the same or different and each represents a hydrogen atom, formyl,

substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted aryloxy carbonyl, a substituted or unsubstituted aliphatic heterocyclic group, a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl), or substituted or unsubstituted aromatic heterocyclic carbonyl (wherein an aromatic heterocyclic moiety of the aromatic heterocyclic carbonyl is not tetrazolyl), or  $R^{11a}$  and  $R^{11b}$  are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted heterocyclic group],

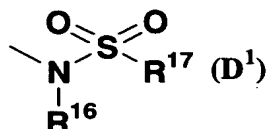
(xiii)  $-OR^{12}$  [wherein  $R^{12}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted aryloxy carbonyl, a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl), substituted or

unsubstituted aromatic heterocyclic oxycarbonyl (wherein an aromatic heterocyclic moiety of the aromatic heterocyclic oxycarbonyl is not tetrazolyl), substituted or unsubstituted lower alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted aromatic heterocyclic sulfonyl (wherein an aromatic heterocyclic moiety of the aromatic heterocyclic sulfonyl is not tetrazolyl), or  $-C(=O)NR^{13a}R^{13b}$  (wherein  $R^{13a}$  and  $R^{13b}$  have the same definitions as  $R^{11a}$  and  $R^{11b}$  described above, respectively)],

(xiv) formula (C<sup>1</sup>)

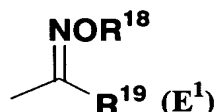


(wherein  $R^{14}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, or substituted or unsubstituted aroyl, and  $R^{15a}$  and  $R^{15b}$  have the same definitions as  $R^{11a}$  and  $R^{11b}$  described above, respectively),  
 (xv) formula (D<sup>1</sup>)



(wherein  $\text{R}^{16}$  has the same definition as  $\text{R}^{14}$  described above, and  $\text{R}^{17}$  represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted aralkyl),

(xvi) formula ( $\text{E}^1$ )



[wherein  $\text{R}^{18}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl), and  $\text{R}^{19}$  has the same definition as  $\text{R}^{17}$  described above],

(xvii)  $-\text{C}(=\text{X}^1)-\text{OR}^{20}$  [wherein  $\text{X}^1$  represents an oxygen atom or a sulfur atom, and  $\text{R}^{20}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or

unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl), provided that  $X^1$  represents an oxygen atom,  $R^{20}$  is not a hydrogen atom],

(xviii)  $-C(=X^2)-NR^{21a}R^{21b}$  (wherein  $X^2$  has the same definition as  $X^1$ , and  $R^{21a}$  and  $R^{21b}$  have the same definitions as  $R^{11a}$  and  $R^{11b}$  described above, respectively), or

(xix) formula (B<sup>1</sup>)



{wherein  $E=F$  represents  $CR^9=CR^{10}$  [wherein  $R^9$  and  $R^{10}$  are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl)] or  $C\equiv C$ ,  $R^8$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, a substituted or

unsubstituted aromatic heterocyclic group (excluding tetrazolyl), or  $-C(R^{A1})(R^{A2})NR^{B1}R^{B2}$  [wherein  $R^{A1}$  and  $R^{A2}$  are the same or different and each represents a hydrogen atom, halogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl),  $R^{A1}$  and  $R^{A2}$  are combined together with the adjacent carbon atom thereto to form a saturated aliphatic ring, or  $R^{A1}$  and  $R^{A2}$  are combined together to represent an oxygen atom or a sulfur atom, and  $R^{B1}$  and  $R^{B2}$  have the same definitions as  $R^{11a}$  and  $R^{11b}$  described above, respectively]]] or a pharmaceutically acceptable salt thereof.

2. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 1, wherein T is formula ( $F^1$ ):

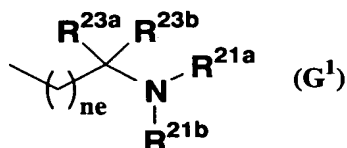


[wherein nd represents an integer of 0 to 3,  $R^{22a}$  and  $R^{22b}$  are the same or different and each represents a hydrogen atom, halogen, substituted or unsubstituted lower



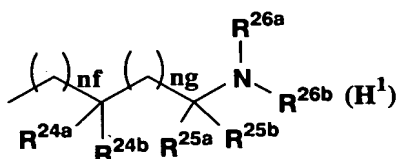
alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl),  $R^{22a}$  and  $R^{22b}$  are combined together with the adjacent carbon atom thereto to form a saturated aliphatic ring, or  $R^{22a}$  and  $R^{22b}$  are combined together to represent an oxygen atom or a sulfur atom, and  $R^{20}$  has the same definition as described above, provided that  $R^{22a}$  and  $R^{22b}$  are combined together to represent an oxygen atom,  $R^{20}$  is not a hydrogen atom].

3. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 1, wherein T is formula ( $G^1$ ):



(wherein ne represents an integer of 0 to 3,  $R^{21a}$  and  $R^{21b}$  have the same definition as described above, respectively, and  $R^{23a}$  and  $R^{23b}$  have the same definitions as  $R^{22a}$  and  $R^{22b}$  described above, respectively).

4. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 3, wherein  $R^{21a}$  and  $R^{21b}$  are the same or different and both or either of  $R^{21a}$  and  $R^{21b}$  is formula ( $H^1$ ):



[wherein nf represents an integer of 0 to 5;

ng represents an integer of 0 to 3;

$R^{24a}$  and  $R^{24b}$  are the same or different and each represents a hydrogen atom, formyl, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl),  $R^{24a}$  and  $R^{24b}$  are combined together with the adjacent carbon atom thereto to form a saturated aliphatic ring, or  $R^{24a}$  and  $R^{24b}$  are combined together to represent an oxygen atom or a sulfur atom;

$R^{25a}$  and  $R^{25b}$  are the same or different and each represents a hydrogen atom, formyl, substituted or

unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl),  $R^{25a}$  and  $R^{25b}$  are combined together with the adjacent carbon atom thereto to form a saturated aliphatic ring,  $R^{25a}$  and  $R^{25b}$  are combined together to represent an oxygen atom or a sulfur atom, or  $R^{25a}$  or  $R^{25b}$  are combined together with  $R^{26a}$  or  $R^{26b}$  and the adjacent carbon atom and nitrogen atom thereto to form a substituted or unsubstituted heterocyclic group;

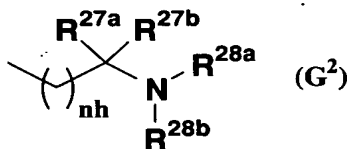
and  $R^{26a}$  and  $R^{26b}$  are the same or different and each represents a hydrogen atom, formyl, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl),  $R^{26a}$  and  $R^{26b}$  are combined together with the adjacent nitrogen atom

thereto to form a substituted or unsubstituted heterocyclic group, or  $R^{26a}$  or  $R^{26b}$  are combined together with  $R^{25a}$  or  $R^{25b}$  and the adjacent nitrogen atom and carbon atom thereto to form a substituted or unsubstituted heterocyclic group].

5. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 1, wherein T is formula ( $B^2$ ):

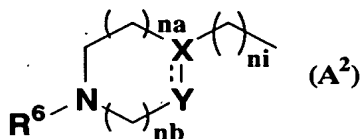


[wherein  $E-F$  has the same definition as described above, and  $R^{8a}$  is formula ( $G^2$ ):



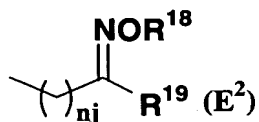
(wherein  $nh$ ,  $R^{27a}$ ,  $R^{27b}$ ,  $R^{28a}$ , and  $R^{28b}$  have the same definitions as  $nd$ ,  $R^{A1}$ ,  $R^{A2}$ ,  $R^{B1}$ , and  $R^{B2}$  described above, respectively)].

6. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 1, wherein T is formula ( $A^2$ ):



(wherein  $ni$  represents an integer of 0 to 2, and  $na$ ,  $nb$ ,  $X$ ,  $Y$ , and  $R^6$  have the same definitions as described above, respectively).

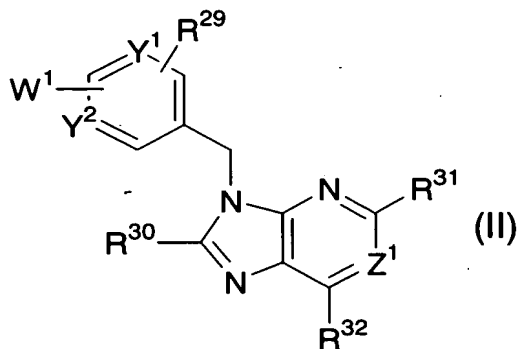
7. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 1, wherein T is formula (E<sup>2</sup>):



(wherein nj represents an integer of 0 to 3, and R<sup>18</sup> and R<sup>19</sup> have the same definitions as described above, respectively).

8. A GPR4 antagonist which comprises, as an active ingredient, the bicyclic heterocyclic compound or pharmaceutically acceptable salt thereof described in any of Claims 1 to 7.

9. A preventive and/or therapeutic agent for neutrophilic inflammatory diseases which comprises, as an active ingredient, a bicyclic heterocyclic compound represented by formula (II):



{wherein Y<sup>1</sup> and Y<sup>2</sup> are the same or different and each represents CH or a nitrogen atom;

W<sup>1</sup> has the same definition as T described above;

Z<sup>1</sup> represents a nitrogen atom or CR<sup>33</sup> [wherein R<sup>33</sup>

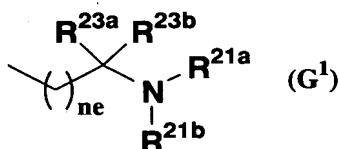
represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl)];

$R^{29}$  represents a hydrogen atom, halogen, amino, nitro, cyano, carboxy, lower alkoxycarbonylamino, mono- or di-lower alkylamino, lower alkylsulfonyl, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, or a substituted or unsubstituted aliphatic heterocyclic group;

and  $R^{30}$ ,  $R^{31}$ , and  $R^{32}$  are the same or different and each represent a hydrogen atom, halogen, cyano, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or

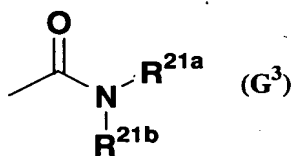
unsubstituted aroyl, a substituted or unsubstituted aliphatic heterocyclic group, or a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl)) or a pharmaceutically acceptable salt thereof.

10. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is formula ( $G^1$ ):



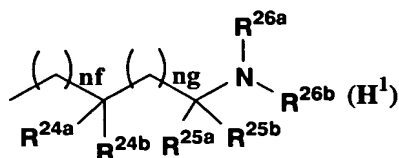
(wherein  $ne$ ,  $R^{21a}$ ,  $R^{21b}$ ,  $R^{23a}$ , and  $R^{23b}$  have the same definitions as described above, respectively).

11. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is formula ( $G^3$ ):



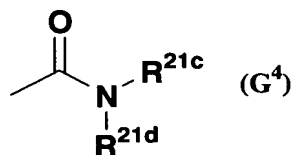
(wherein  $R^{21a}$  and  $R^{21b}$  have the same definitions described above, respectively).

12. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 10 or 11, wherein  $R^{21a}$  and  $R^{21a}$  are the same or different and both or either of  $R^{21a}$  and  $R^{21a}$  is formula ( $H^1$ ):



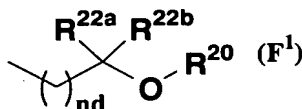
(wherein nf, ng, R<sup>24a</sup>, R<sup>24b</sup>, R<sup>25a</sup>, R<sup>25b</sup>, R<sup>26a</sup>, and R<sup>26b</sup> have the same definitions as described above, respectively).

13. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein W<sup>1</sup> is formula (G<sup>4</sup>):



(wherein R<sup>21c</sup> and R<sup>21d</sup> are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted aralkyl, or R<sup>21c</sup> and R<sup>21d</sup> are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted heterocyclic group).

14. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein W<sup>1</sup> is formula (F<sup>1</sup>):



(wherein nd, R<sup>20</sup>, R<sup>22a</sup>, and R<sup>22b</sup> have the same definitions as described above, respectively).



15. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is formula ( $B^2$ ):



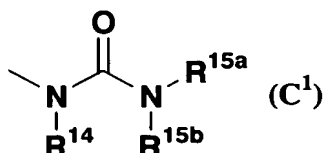
(wherein  $\text{E--F}$  and  $R^{8a}$  have the same definitions as described above, respectively).

16. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is  $\text{---NR}^{11a}\text{R}^{11b}$  (wherein  $R^{11a}$  and  $R^{11b}$  have the same definitions as described above, respectively).

17. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is  $\text{---NHR}^{11a}$  (wherein  $R^{11a}$  has the same definition as described above).

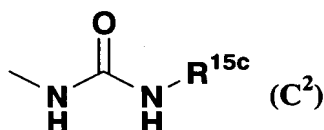
18. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is  $\text{---NHR}^{11c}$  [wherein  $R^{11c}$  represents substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower cycloalkylcarbonyl, substituted or unsubstituted aroyl, or substituted or unsubstituted aromatic heterocyclic carbonyl (wherein an aromatic heterocyclic moiety of the aromatic heterocyclic carbonyl is not tetrazolyl)].

19. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is formula ( $C^1$ ):



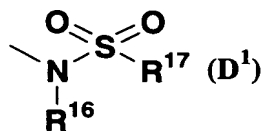
(wherein  $\text{R}^{14}$ ,  $\text{R}^{15a}$ , and  $\text{R}^{15b}$  have the same definitions as described above, respectively).

20. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $\text{W}^1$  is formula ( $\text{C}^2$ ):



(wherein  $\text{R}^{15c}$  represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted aralkyl).

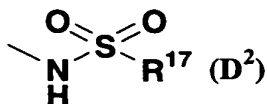
21. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $\text{W}^1$  is formula ( $\text{D}^1$ ):



(wherein  $\text{R}^{16}$  and  $\text{R}^{17}$  have the same definitions as described above, respectively).

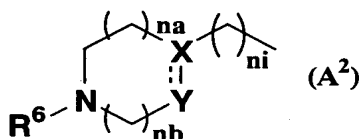
22. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $\text{W}^1$  is

formula ( $D^2$ ):



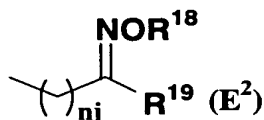
(wherein  $R^{17}$  has the same definition as described above).

23. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein W<sup>1</sup> is formula (A<sup>2</sup>):



(wherein na, nb, ni, X--Y, and R<sup>6</sup> have the same definitions as described above, respectively).

24. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to Claim 9, wherein  $W^1$  is formula ( $E^2$ ):



(wherein  $n_j$ ,  $R^{18}$ , and  $R^{19}$  have the same definitions as described above, respectively).

25. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 24, wherein R<sup>29</sup> is a hydrogen atom.

26. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 25,

wherein  $R^{30}$ ,  $R^{31}$ , and  $R^{32}$  are the same or different and each represents a hydrogen atom, halogen, or substituted or unsubstituted lower alkyl.

27. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 26, wherein  $Z^1$  is  $CR^{33}$  (wherein  $R^{33}$  has the same definition as described above).

28. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 26, wherein  $Z^1$  is CH.

29. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 28, wherein  $Y^1$  and  $Y^2$  are CH.

30. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 28, wherein  $Y^1$  and  $Y^2$  are a nitrogen atom.

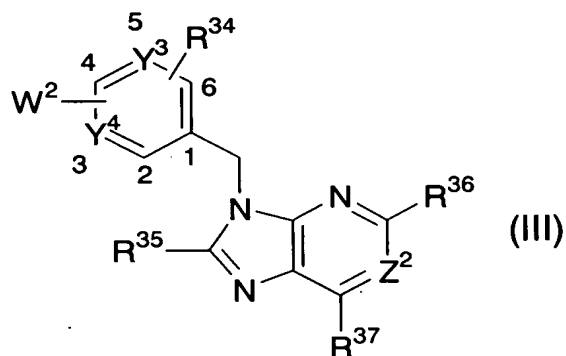
31. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 30, wherein  $R^{30}$ ,  $R^{31}$ , and  $R^{32}$  are the same or different and each represents a hydrogen atom or substituted or unsubstituted lower alkyl.

32. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 9 to 30, wherein  $R^{30}$  and  $R^{32}$  are the same or different and each represents a hydrogen atom or substituted or unsubstituted

lower alkyl, and  $R^{31}$  represents halogen.

33. A GPR4 antagonist which comprises, as an active ingredient, the bicyclic heterocyclic compound or pharmaceutically acceptable salt thereof described in any of Claims 9 to 32.

34. A bicyclic heterocyclic compound represented by formula (III):



{wherein  $Y^3$  and  $Y^4$  have the same definitions as  $Y^1$  and  $Y^2$  described above, respectively;

$W^2$  is bonded at the 3-, 4-, or 5-position of a benzene ring and represents:

(i) formyl;

(ii) lower alkyl or lower alkyl substituted by 1 to 3 substituents which are the same or different and selected from the following substituent group A [substituent group A: halogen, hydroxy, formyl, trifluoromethyl, vinyl, styryl, phenylethynyl, lower cycloalkyl, lower alkoxy, hydroxy-substituted lower alkoxy, lower alkoxy-substituted lower alkoxy, lower alkoxycarbonyl, lower alkanoyl, aryl-

substituted lower alkanoyl, aryloxy, aralkyloxy, aroyl, a substituted or unsubstituted aliphatic heterocyclic group, a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl)];

(iii) substituted or unsubstituted lower cycloalkyl;

(iv) substituted or unsubstituted lower alkanoyl;

(v) substituted or unsubstituted lower cycloalkylcarbonyl;

(vi) substituted or unsubstituted aryl;

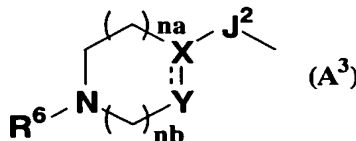
(vii) substituted or unsubstituted aralkyl;

(viii) substituted or unsubstituted aroyl;

(ix) a substituted or unsubstituted aromatic heterocyclic group (excluding tetrazolyl);

(x) substituted or unsubstituted aromatic heterocyclic carbonyl (wherein an aromatic heterocyclic moiety of the aromatic heterocyclic carbonyl is not tetrazolyl);

(xi) formula (A<sup>3</sup>):

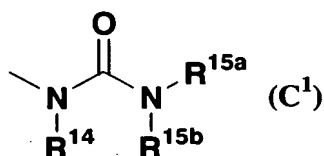


[wherein na, nb, R<sup>6</sup>, and X--Y have the same definitions as described above, respectively, and J<sup>2</sup> represents a single bond, carbonyl, -CH<sub>2</sub>-, or -(CH<sub>2</sub>)<sub>2</sub>-];

(xii) -NR<sup>11a</sup>R<sup>11b</sup> (wherein R<sup>11a</sup> and R<sup>11b</sup> have the same definitions as described above, respectively);

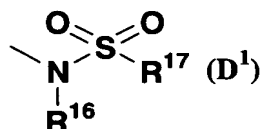
(xiii)  $-OR^{12}$  (wherein  $R^{12}$  has the same definition as described above);

(xiv) formula (C<sup>1</sup>):



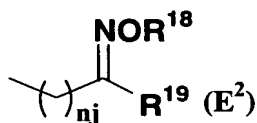
(wherein  $R^{14}$ ,  $R^{15a}$ , and  $R^{15b}$  have the same definitions as described above, respectively);

(xv) formula (D<sup>1</sup>):



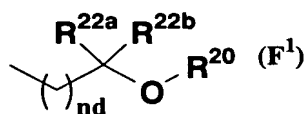
(wherein  $R^{16}$  and  $R^{17}$  have the same definitions as described above, respectively);

(xvi) formula (E<sup>2</sup>):



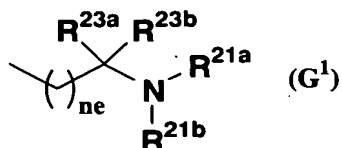
(wherein  $n_j$ ,  $R^{18}$ , and  $R^{19}$  have the same definitions as described above, respectively);

(xvii) formula (F<sup>1</sup>):



(wherein  $n_d$ ,  $R^{20}$ ,  $R^{22a}$ , and  $R^{22b}$  have the same definitions as described above, respectively);

(xviii) formula (G<sup>1</sup>):



(wherein ne, R<sup>21a</sup>, R<sup>21b</sup>, R<sup>23a</sup>, and R<sup>23b</sup> have the same definitions as described above, respectively); or

(xix) formula (B<sup>1</sup>):



(wherein E--F and R<sup>8</sup> have the same definitions as described above, respectively);

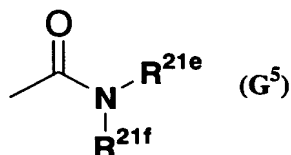
R<sup>34</sup>, R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup>, and Z<sup>2</sup> have the same definitions as R<sup>29</sup>, R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, and Z<sup>1</sup> described above, respectively;

Provided that Z<sup>2</sup> is a nitrogen atom, R<sup>35</sup> is a hydrogen atom or lower alkyl, R<sup>36</sup> and R<sup>37</sup> are each a hydrogen atom, lower alkyl, or an aliphatic heterocyclic group, and R<sup>34</sup> is lower alkoxy or halogen-substituted lower alkoxy, W<sup>2</sup> is not -OR<sup>12a</sup> (wherein R<sup>12a</sup> represents lower alkyl, halogen-substituted lower alkyl, or lower cycloalkyl);

Z<sup>2</sup> is a nitrogen atom or CH, R<sup>35</sup> is a hydrogen atom, one of R<sup>36</sup> and R<sup>37</sup> is a hydrogen atom, the other is a hydrogen atom, lower alkyl, or aryl, and R<sup>34</sup> is a hydrogen atom or amino, W<sup>2</sup> is neither amino nor hydroxy;

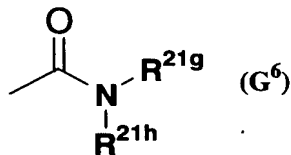
Z<sup>2</sup> is a nitrogen atom, R<sup>35</sup>, R<sup>36</sup>, and R<sup>37</sup> are each a hydrogen atom, and R<sup>34</sup> is a hydrogen atom, halogen, lower alkoxy, or substituted or unsubstituted lower alkyl, W<sup>2</sup> is not formula (G<sup>5</sup>):





[wherein  $\text{R}^{21\text{e}}$  and  $\text{R}^{21\text{f}}$  are the same or different and each represents lower alkyl, (substituted or unsubstituted lower cycloalkyl)-substituted lower alkyl, lower cycloalkyl, or lower alkyl-substituted lower cycloalkyl]; and

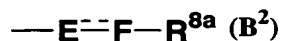
$\text{Z}^2$  is  $\text{CR}^{33\text{a}}$  (wherein  $\text{R}^{33\text{a}}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted lower alkanoyl, or substituted or unsubstituted aralkyl),  $\text{W}^2$  is not formula ( $\text{G}^6$ ):



[wherein  $\text{R}^{21\text{g}}$  and  $\text{R}^{21\text{h}}$  are the same or different and each represents a hydrogen atom, lower alkyl, halogen-substituted lower alkyl, lower alkoxy-substituted lower alkyl, lower cycloalkyl, lower cycloalkyl substituted by 1 to 3 substituents selected from the substituent group B described below (substituent group B: halogen, lower alkyl, halogen-substituted lower alkyl, and lower alkoxy), aryl, aryl substituted by 1 to 3 substituents selected from the substituent group B described above, aralkyl, or aralkyl substituted by 1 to 3 substituents selected from the

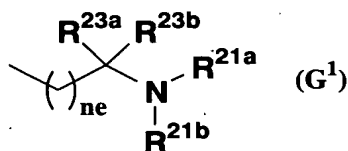
substituent group B described above]] or a pharmaceutically acceptable salt thereof.

35. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula ( $B^2$ ):



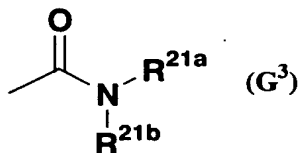
(wherein  $E-F$  and  $R^{8a}$  have the same definitions as described above, respectively).

36. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula ( $G^1$ ):



(wherein  $ne$ ,  $R^{21a}$ ,  $R^{21b}$ ,  $R^{23a}$ , and  $R^{23b}$  have the same definitions as described above, respectively).

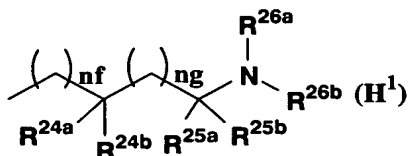
37. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula ( $G^3$ ):



(wherein  $R^{21a}$  and  $R^{21b}$  have the same definitions as described above, respectively).

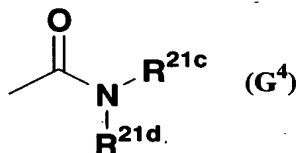
38. The bicyclic heterocyclic compound or the

pharmaceutically acceptable salt thereof according to Claim 36 or 37, wherein  $R^{21a}$  and  $R^{21b}$  are the same or different and both or either of  $R^{21a}$  and  $R^{21b}$  is formula ( $H^1$ ):



(wherein nf, ng,  $R^{24a}$ ,  $R^{24b}$ ,  $R^{25a}$ ,  $R^{25b}$ ,  $R^{26a}$ , and  $R^{26b}$  have the same definitions as described above, respectively).

39. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula ( $G^4$ ):



(wherein  $R^{21c}$  and  $R^{21d}$  have the same definitions as described above, respectively).

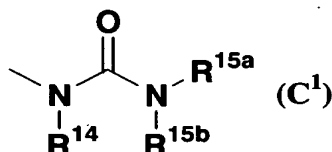
40. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is  $-NR^{11a}R^{11b}$  (wherein  $R^{11a}$  and  $R^{11b}$  have the same definitions as described above, respectively).

41. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is  $-NHR^{11a}$  (wherein  $R^{11a}$  has the same definition as described above).

42. The bicyclic heterocyclic compound or the

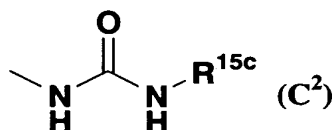
pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is  $-NHR^{11c}$  (wherein  $R^{11c}$  has the same definition as described above).

43. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula (C<sup>1</sup>):



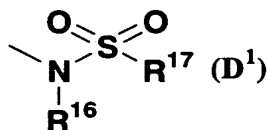
(wherein  $R^{14}$ ,  $R^{15a}$ , and  $R^{15b}$  have the same definitions as described above, respectively).

44. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula (C<sup>2</sup>):



(wherein  $R^{15c}$  has the same definition as described above).

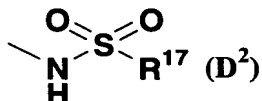
45. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula (D<sup>1</sup>):



(wherein  $R^{16}$  and  $R^{17}$  have the same definitions as described

above, respectively).

46. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is formula ( $D^2$ ):



(wherein  $R^{17}$  has the same definition as described above).

47. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to Claim 34, wherein  $W^2$  is  $-NHR^{11d}$  (wherein  $R^{11d}$  represents substituted or unsubstituted lower cycloalkylcarbonyl).

48. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 47, wherein  $R^{34}$  is a hydrogen atom.

49. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 48, wherein  $R^{35}$ ,  $R^{36}$ , and  $R^{37}$  are the same or different and each is a hydrogen atom, halogen, or substituted or unsubstituted lower alkyl.

50. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 49, wherein  $Z^2$  is  $CR^{33}$  (wherein  $R^{33}$  has the same definition as described above).

51. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of

Claims 34 to 49, wherein  $Z^2$  is CH.

52. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 51, wherein  $Y^3$  and  $Y^4$  are CH.

53. The bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 51, wherein  $Y^3$  and  $Y^4$  are a nitrogen atom.

54. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 34 to 53, wherein  $R^{35}$ ,  $R^{36}$ , and  $R^{37}$  are the same or different and each represents a hydrogen atom or substituted or unsubstituted lower alkyl.

55. The preventive and/or therapeutic agent for neutrophilic inflammatory diseases according to any of Claims 34 to 53, wherein  $R^{35}$  and  $R^{37}$  are the same or different and each represents a hydrogen atom or substituted or unsubstituted lower alkyl, and  $R^{36}$  represents halogen.

56. A pharmaceutical composition which comprises, as an active ingredient, the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55.

57. A GPR4 antagonist which comprises, as an active ingredient, the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55.

58. A preventive and/or therapeutic agent for neutrophilic inflammatory diseases which comprises, as an active ingredient, the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55.

59. A preventive and/or therapeutic agent for diseases derived from hyperfunction of GPR4 which comprises, as an active ingredient, the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 1 to 7.

60. A preventive and/or therapeutic agent for diseases derived from hyperfunction of GPR4 which comprises, as an active ingredient, the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 9 to 32.

61. A preventive and/or therapeutic agent for diseases derived from hyperfunction of GPR4 which comprises, as an active ingredient, the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55.

62. A method for preventing and/or treating neutrophilic inflammatory diseases, which comprises a step of administering an effective amount of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 1 to 7.

63. A method for preventing and/or treating diseases derived from hyperfunction of GPR4, which comprises a step of administering an effective amount of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 1 to 7.

64. A method for preventing and/or treating neutrophilic inflammatory diseases, which comprises a step of administering an effective amount of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 9 to 32.

65. A method for preventing and/or treating diseases derived from hyperfunction of GPR4, which comprises a step of administering an effective amount of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 9 to 32.

66. A method for preventing and/or treating neutrophilic inflammatory diseases, which comprises a step of administering an effective amount of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55.

67. A method for preventing and/or treating diseases derived from hyperfunction of GPR4, which comprises a step of administering an effective amount of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55.



68. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 1 to 7 for the manufacture of a preventive and/or therapeutic agent for neutrophilic inflammatory diseases.

69. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 1 to 7 for the manufacture of a GPR4 antagonist.

70. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 1 to 7 for the manufacture of a preventive and/or therapeutic agent for diseases derived from hyperfunction of GPR4.

71. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 9 to 33 for the manufacture of a preventive and/or therapeutic agent for neutrophilic inflammatory diseases.

72. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 9 to 33 for the manufacture of a GPR4 antagonist.

73. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof described in any of Claims 9 to 33 for the manufacture of a preventive and/or therapeutic agent for diseases derived from hyperfunction of GPR4.

74. Use of the bicyclic heterocyclic compound or the

pharmaceutically acceptable salt thereof according to any of Claims 34 to 55 for the manufacture of a preventive and/or therapeutic agent for neutrophilic inflammatory diseases.

75. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55 for the manufacture of a GPR4 antagonist.

76. Use of the bicyclic heterocyclic compound or the pharmaceutically acceptable salt thereof according to any of Claims 34 to 55 for the manufacture of a preventive and/or therapeutic agent for diseases derived from hyperfunction of GPR4.